

**Report on Evaluation of Safety, Efficacy and Quality of
Comirnaty COVID-19 mRNA Vaccine (BNT162b2) Concentrate
for Dispersion for Injection**

BACKGROUND

In view of the pandemic of COVID-19, the Government strives to provide sufficient supplies of vaccines for the Hong Kong population as early as possible. To expedite and allow early use of the vaccines, the Government published the Prevention and Control of Disease (Use of Vaccines) Regulation (“the Regulation”), Cap. 599K, Laws of Hong Kong, in the Gazette on 23 December 2020. The Regulation provides the legal framework under the present state of public health emergency to bring in COVID-19 vaccines which satisfy the criteria of safety, efficacy and quality for emergency use in Hong Kong.

2. The Regulation empowers the Secretary for Food and Health to authorize and allow the specified use of a COVID-19 vaccine in Hong Kong under the emergency situation, which is basically for vaccination programmes conducted by the Government, having regard to the objective clinical data of the COVID-19 vaccine (including Phase 3 clinical research data), the expert advice of an independent advisory panel and the approval given by a regulatory authority in a place outside Hong Kong that performs the function of approving pharmaceutical products (including emergency use).

3. The Advisory Panel on COVID-19 Vaccines (“the Advisory Panel”), as appointed by the Chief Executive, was established to provide expert advice to the Secretary for Food and Health in relation to the safety, efficacy, and quality of a COVID-19 vaccine under application for authorization under the Regulation. The Advisory Panel is also responsible for advising the Secretary for Food and Health on the conditions to be attached to an authorization and revocation of an authorization.

APPLICATION FOR AUTHROIZATION

4. On 4 January 2021, an application for authorization under the Regulation was received by the Secretary for Food and Health. Details of the vaccine under application are summarized below:

Name of Vaccine:	Comirnaty COVID-19 mRNA Vaccine (BNT162b2) Concentrate for Dispersion for Injection
Name and Address of Applicant:	Fosun Industrial Co., Limited Level 54, Hopewell Centre, 183 Queen’s Road East, Hong Kong

<p>Name and Address of Manufacturer:</p>	<p>BioNTech Manufacturing GmbH Kupferbergterrasse 17-19, Mainz, Rheinland-Pfalz, 55116, Germany</p>
<p>Composition:</p>	<p>Each vial (0.45ml) contains 5 doses*¹ of 30 micrograms of COVID-19 mRNA vaccine (embedded in lipid nanoparticles).</p> <p>The vaccine is single-stranded, 5'-capped mRNA produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2.</p> <p>The vaccine also contains the following excipients:</p> <p>((4-hydroxybutyl) azanediyl) bis (hexane-6,1-diyl) bis(2-hexyldecanoate) (ALC-0315), 2-[(polyethylene glycol)-2000]-N, N-ditetradecylacetamide (ALC-0159), 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC), cholesterol, potassium chloride, potassium dihydrogen phosphate, sodium chloride, disodium hydrogen phosphate dihydrate, sucrose, water for injections</p>
<p>Therapeutic Indications:</p>	<p>Active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 16 years of age and older.</p> <p>The use of the vaccine should be in accordance with the official recommendations.</p>
<p>Contraindication</p>	<p>Hypersensitivity to the active substance or to any of the excipient.</p>
<p>Posology</p>	<p><i>Individuals of 16 years of age and older</i></p> <p>The vaccines is administered intramuscularly after dilution as a series of two doses (0.3ml each) at least 21 days apart.</p> <p>There is no data available on the interchangeability of Comirnaty with other COVID-19 vaccines to complete the vaccination course. Individuals who have received 1 dose of Comirnaty should receive a second dose of Comirnaty to complete the vaccination course.</p>

1 It is noted a 6 doses/vial preparation will be available for supply to Hong Kong provided that low dead-volume syringes/needles (with dead-volume no more than 35 microliters) is available. The relevant labels and package insert information will be updated when 6 doses/vial is to be supplied.

	<p><i>Paediatric population</i></p> <p>The safety and efficacy of Comirnaty in children and adolescents aged less than 16 years of age have not yet been established. Limited data is available.</p> <p><i>Elderly population</i></p> <p>No dosage adjustment is required in elderly individuals ≥ 65 years of age.</p>
Precautions for Use	<p><i>Hypersensitivity and anaphylaxis</i></p> <p>Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.</p> <p>Close observation for at least 15 minutes is recommended following vaccination. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of Comirnaty.</p> <p><i>Anxiety-related reactions</i></p> <p>Anxiety-related reactions, including vasovagal reaction (syncope), hyperventilation or stress-related reaction may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.</p> <p><i>Concurrent illness</i></p> <p>Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.</p> <p><i>Thrombocytopenia and coagulation disorders</i></p> <p>As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.</p>

	<p><i>Immunocompromised individuals</i></p> <p>The efficacy, safety and immunogenicity of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of Comirnaty may be lower in immunosuppressed individuals.</p> <p><i>Duration of protection</i></p> <p>The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical trials.</p> <p><i>Limitation of vaccine effectiveness</i></p> <p>As with any vaccine, vaccination with Comirnaty may not protect all vaccine recipients. Individuals may not be fully protected until 7 days after their second dose of vaccine.</p>
<p>Interaction with other medicinal products and other forms of interaction</p>	<p>No interaction studies have been performed.</p> <p>Concomitant administration of Comirnaty with other vaccines has not been studied.</p>
<p>Information on Fertility, Pregnancy and Lactation</p>	<p><i>Pregnancy</i></p> <p>There is limited experience with use of Comirnaty in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development. Administration of Comirnaty in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.</p> <p><i>Breast-feeding</i></p> <p>It is unknown whether Comirnaty is excreted in human milk.</p> <p><i>Fertility</i></p> <p>Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.</p>
<p>Vaccine Platform and Mechanism of action:</p>	<p>mRNA vaccine</p> <p>The nucleoside-modified mRNA in Comirnaty is formulated in lipid nanoparticles, which enable delivery of the non replicating RNA into host cells to direct transient expression</p>

	<p>of the SARS-CoV-2 S antigen. The mRNA codes for membrane-anchored, full-length S with two point mutations within the central helix. Mutation of these two amino acids to proline locks S in an antigenically preferred prefusion conformation. The vaccine elicits both neutralizing antibody and cellular immune responses to the spike (S) antigen, which may contribute to protection against COVID-19.</p>
<p>Shelf Life</p>	<p><i>Unopened vial</i></p> <p>Unopened vial can be stored in a freezer at -90°C to -60°C for 6 months.</p> <p>Once removed from the freezer, the unopened vaccine can be stored for up to 5 days at 2°C to 8°C, and up to 2 hours at temperature up to 30°C, prior to use.</p> <p>Once thawed, the vaccine should not be re-frozen.</p> <p>Close-lid vial trays containing 195 vials removed from frozen stage (<-60°C) may be at room temperature (<25°C) for up to 5 minutes for transfer between ultra-low-temperature environments.</p> <p>After vial trays are returned to frozen storage following room temperature exposure, they must remain in frozen storage for at least 2 hours before they can be removed again.</p> <p><i>Diluted medicinal product</i></p> <p>Chemical and physical in-use stability has been demonstrated for 6 hours at 2°C to 30°C after dilution in sodium chloride 9 mg/mL (0.9%) solution for injection. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.</p>
<p>Special Precautions for Storage</p>	<p>Store in a freezer at -90°C to -60°C.</p> <p>Store in the original package in order to protect from light.</p> <p>During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.</p> <p>Thawed vials can be handled in room light conditions.</p> <p>When the vaccines are ready to thaw or use:</p>

	<ul style="list-style-type: none"> - Open-lid vial trays, or vial trays containing less than 195 vials removed from frozen storage (<-60°C) may be at room temperature (<25°C) for up to 3 minutes to remove vials or for transfer between ultra-low-temperature environments. - Once a vial is removed from the vial tray, it should be thawed for use. <p>After the vial trays are returned to frozen storage following room temperature exposure, they must remain in frozen storage for at least 2 hours before they can be removed again.</p>
<p>Handling Instructions</p>	<p>Comirnaty should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared dispersion.</p> <p>The multidose vials are stored frozen and must be thawed prior to dilution. Frozen vials should be transferred to an environment of 2°C to 8°C to thaw; a 195 vial pack may take 3 hours to thaw. Alternatively, frozen vials may also be thawed for 30 minutes at temperatures up to 30°C for immediate use.</p> <p>The thawed vaccine must be diluted in its original vial with 1.8mL sodium chloride 9mg/mL (0.9%) solution for injection. After dilution, the vial contains 2.25mL corresponding to 5 doses of 0.3mL.</p> <p>The vaccine should be used within 6 hours at (2°C to 30°C) after dilution. Any unused medicinal product or waste materials should be disposed accordingly.</p> <p><i>The package insert contains further details on handling instruction.</i></p>
<p>Packaging Information</p>	<p>195 vials per box</p> <p>5 vials per box</p> <p>1 vial per box</p>
<p>Approval by Other Regulatory Authority(ies):</p>	<ul style="list-style-type: none"> • Medicines and Healthcare products Regulatory Agency (the United Kingdom (“UK”)), authorisation for the

	<p>temporary supply of the vaccine granted on 2 December 2020</p> <ul style="list-style-type: none">• Health Canada (Canada), Interim Order Authorization granted on 9 December 2020• Food and Drug Administration (the United States (“US”)), Emergency Use Authorization for emergency use granted on 11 December 2020• Health Science Authority (Singapore), Interim Authorisation granted on 14 December 2020• Swissmedic (Switzerland), Marketing Authorization with Conditions granted on 19 December 2020• European Medicines Agency (the European Union (“EU”)), Conditional Marketing Authorization granted on 21 December 2020• World Health Organization, Emergency Use Listing on 31 December 2020 (by taking reference to European Medicines Agency marketing authorization)• Other regulatory authorities of Bahrain, Israel, Saudi Arabia, Mexico, Kuwait, Oman, Lebanon, Panama, Chile, Costa Rica, Ecuador, Qatar, Norway, Argentina, Iceland, Serbia.
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SAFETY, EFFICACY AND QUALITY OF COMIRNATY

5. The Advisory Panel conducted its meeting on 18 January 2021 to review the safety, efficacy and quality of Comirnaty by taking into consideration of the submission from the applicant, published information, approval or authorization details and/or assessment results of overseas drug regulatory authorities, and post-marketing information (including a Summary Monthly Safety Report covering the period of 1 December 2020 through 31 December 2020). The Advisory Panel noted the following:

Vaccine Details

- Comirnaty is a concentrate for dispersion for injection and is to be administered intramuscularly after dilution as a course of 2 doses (0.3ml each) at least 21 days

apart. It is used for active immunization to prevent COVID-19 caused by SARS-CoV-2 virus in individual 16 years or age and older;

- the vaccine contains nucleoside-modified messenger RNA formulated in lipid nanoparticles, which enable delivery of the non replicating RNA into host cells to direct transient expression of the SARS-CoV-2 S antigen. The mRNA codes for membrane-anchored, full-length S with two point mutations within the central helix. Mutation of these two amino acids to proline locks S in an antigenically preferred prefusion conformation. The vaccine elicits both neutralizing antibody and cellular immune responses to the spike (S) antigen, which may contribute to protection against COVID-19;
- the vaccine also contains excipients listed below: ((4-hydroxybutyl) azanediyl)bis (hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315), 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159), 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC), cholesterol, potassium chloride, potassium dihydrogen phosphate, sodium chloride, disodium hydrogen phosphate dehydrate, sucrose, water for injections;

Efficacy

- a large scale Phase 3 placebo-controlled study involving **around 44 000 subjects**, with the data cut-off date for final efficacy analysis up to 14 November 2020, showed that Comirnaty was effective at preventing COVID-19 in **people from 16 years of age**;
- vaccine efficacy was evaluated in over 36 000 subjects from 16 years of age who had no evidence of past COVID-19 infection. **The vaccine efficacy was 95%** meaning a 95% reduction in the number of symptomatic COVID-19 cases in people who received the vaccine (8 cases out of 18 198 got COVID-19 symptoms) compared with people who received the placebo (162 cases out of 18 325 got COVID-19 symptoms). The results were also consistent across various subgroups by age, sex, race/ethnicity, and country of clinical trial with vaccine efficacy >90% in almost all analyses;
- for severe COVID-19 cases, the vaccine efficacy was 66.4% (1 severe COVID-19 case in vaccine group and 3 cases in placebo group) but the result did not meet the prespecified success criterion for statistical analysis. No conclusion can be drawn regarding the efficacy on the prevention of severe COVID-19 due to limited data;

- it is presently unknown regarding the effectiveness of the vaccine in certain populations, such as immunocompromised individuals, individuals previously infected with SARS-CoV-2, and pediatric population; and the effectiveness on protection against asymptomatic infection, viral transmission or mortality;
- the duration of protection is not known yet;

Safety

- the most common adverse reactions of Comirnaty identified in the clinical study included injection site pain, fatigue, headache, myalgia and chills, arthralgia, pyrexia, injection site swelling, nausea, and injection site redness and were usually mild or moderate in intensity and resolved within a few days after vaccination;
- uncommon and rare adverse reactions included lymphadenopathy, insomnia, pain in extremity, malaise, and injection site pruritus that occurred rarely in less than 1 in 100 people, and acute peripheral facial paralysis that occurred in less than 1 in 1 000 people;
- the incidence of anaphylaxis and hypersensitivity cannot be estimated from the available clinical trial data. According to post marketing experience on emergency use of Comirnaty in UK, Canada and US, there were two cases of anaphylactoid reaction out of 138 000 persons vaccinated in one of the countries. The subjects were EpiPen user, and the reactions were resolved with standard therapy. Another case of anaphylaxis was reported in another country in a subject without known history of allergies, which required admission to Intensive Care Unit (“ICU”) and was then resolved. In addition, according to the Morbidity and Mortality Weekly Report issued by US Centers for Disease Control and Prevention, during the period of 14 to 23 December 2020, 21 cases of anaphylaxis after administration of a reported 1 893 360 first doses of Comirnaty (11.1 cases per million doses) were detected and 71% of these occurred within 15 minutes of vaccination;
- the current available post-market adverse event data (as of 31 December 2020) demonstrating there was in general no new significant safety information and the overall benefit risk balance was reported to remain favourable. Those identified risks were considered minimized through provision of relevant product information in the package insert to support safe use of the vaccine;

- specifically for anaphylaxis (an important identified risk) and facial paralysis (a risk under determination, and including Bell's Palsy), in order to mitigate the risks, appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine and a minimal 15 minutes of observation following vaccination would be essential and this information is included in the package insert of Comirnaty. Moreover, a timely and proper medical treatment should be given to subjects when experiencing facial paralysis;
- several death cases in very frail subjects associated with the use of Comirnaty were reported in Europe, such as Norway and Germany. Upon preliminary assessment by the relevant overseas health authorities, **there was no certain connection between the deaths and the vaccines**, though it was considered that common adverse events such as fever and nausea might have contributed to a severe course and fatal outcome in elderly who were frail and with severe underlying disease. The Norwegian health authority, as a result, updated its vaccination guide with more detailed advice on vaccinating for those with severe frailty;
- the Government is advised to seek more details on the demographic, medical condition, underlying diseases, etc. of the above death cases from the applicant and relevant health authorities of Norway and Germany for review on their association with the use of COVID-19 vaccine;
- by taking into consideration of the totality of scientific evidence and the above post-market safety information, the emerging safety profile is presently considered favourable. It is acknowledged that long term safety data and including those used in certain populations (e.g. pregnancy, frail subjects, subjects with pre-existing autoimmune disease, etc.), and information of adverse reactions requiring longer follow up for detection is missing at this stage;

Quality

- the manufacturers of the vaccine, including BioNTech Manufacturing GmbH in Germany is demonstrated to comply with the Pharmaceutical Inspection Cooperation Scheme Good Manufacturing Practice standards or equivalent standards and the quality attributes of Comirnaty aligned with those as approved by the European Medicines Agency;

- the applicant will implement a local logistic plan to ensure the handling and distribution of the vaccine is strictly complied with the storage requirements;
- the European Medicines Agency has imposed various specific obligations for the marketing authorization holder to address the quality development issues and to achieve a more comprehensive data and control of the vaccine, and the applicant will be required to follow suit;
- the Government is strongly advised to conduct or arrange sterility and other appropriate tests on the vaccines to ensure quality of the vaccine;

Risk Management Plan

- the applicant committed to implement a Hong Kong risk management plan which adopted the European Union Risk Management Plan that addressed various important risks and missing information that need further follow up, and they include:
 - o Important identified risks: anaphylaxis;
 - o Important potential risks: vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD);
 - o Missing information: use in pregnancy and while breast feeding, use in immunocompromised patients, use in frail patients with co-morbidities (e.g. chronic obstructive pulmonary disease, diabetes, chronic neurological disease, cardiovascular disorders), use in patients with autoimmune or inflammatory disorders, interaction with other vaccines, and long term safety data;
- the Hong Kong risk management plan is considered sufficient in addressing the risks by conducting related pharmacovigilance and risk minimization measures. The applicant also committed to submit the results of relevant post-authorization study as required by overseas drug regulatory authorities that aims to provide long term efficacy and safety data as well as information on the use of certain specific population to address the unknown data gap. The applicant also committed to provide the periodic safety update report and the summary monthly safety report (with the first one provided) in order to review the post-market safety;
- it is also noted that the Government will put in place a mechanism for monitoring any adverse events occurred to the recipients associated with the administration of the vaccines in Hong Kong;

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- a package insert for healthcare professionals (**Annex A**) and a bilingual patient information leaflet for public (**Annex B**) provided by the applicant that summarized the indication, dosage, precautionary information, adverse events profile and storage condition of the vaccine will be made available for the healthcare professionals and members of the public.

ADVICE OF THE ADVISORY PANEL

6. After deliberation, the Advisory Panel considered that, based on the totality of scientific evidence on safety, efficacy and quality as available and the post-authorization measures to be taken, the benefits of Comirnaty outweigh its risks for use in Hong Kong for active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 16 years of age and older during the current pandemic situation.

CONDITIONS OF AUTHORIZATION

7. The Advisory Panel is of the view that for the purpose to ensure the benefits of Comirnaty continuously outweigh its risk, the applicant is recommended to comply with the following conditions if authorization is granted:

- (a) the authorization applicant is required to report to the Department of Health (“DH”) as soon as possible, and in any event no later than 72 hours after receipt of information, of any actions taken by overseas drug regulatory authorities on the authorized vaccine as a consequence of any safety concern of the authorized vaccine. Such overseas actions include, but are not limited to, the following actions arising from the safety concern of the authorized vaccine:
 - (i) recall, suspension or withdrawal of the authorized vaccine; or
 - (ii) addition or modification for safety reasons of a contraindication, warning or precaution statement in the product information;
- (b) the authorization applicant is required to submit the final reports of all planned, on-going or future clinical studies of the authorized vaccine, which are part of its post-marketing commitments to overseas drug regulatory authorities of Canada, European Union (“EU”), the United Kingdom (“UK”) or the United States (“US”), to the DH for reassessment at the same time when the said reports are submitted to these overseas

drug regulatory authorities. A summary of the conclusion of the clinical studies and the proposed follow-up actions have to be provided. If there are any regulatory actions taken by these overseas drug regulatory authorities in view of the results of the clinical studies of the authorized vaccine, the authorization applicant is required to inform the DH of the actions as soon as possible, and in any event no later than 72 hours after the actions have been taken;

- (c) the authorization applicant is required to submit periodic safety update reports, or their equivalents, of the authorized vaccine to the DH every six months or at an interval as may be notified by the Secretary for Food and Health; and to submit summary safety reports monthly to the DH at the same time when the said reports are submitted to other overseas drug regulatory authorities until notified by the Secretary for Food and Health;
- (d) the authorization applicant is required to report all serious or unexpected adverse events following immunization of the authorized vaccine occurring in Hong Kong to the DH in accordance with available guidance for COVID-19 vaccine;
- (e) the authorization applicant is required to implement the Risk Management Plan (“RMP”) for the authorized vaccine in Hong Kong as it has proposed. The authorization applicant is also required to update the local RMP in accordance with the EU RMP when it is modified and implement accordingly;
- (f) the authorization applicant is required to report to the DH any significant changes or any conditions relating to the manufacturer or to the manufacture of the vaccine which may affect the quality, safety or efficacy of the authorized vaccine without undue delay;
- (g) upon commencement of recall of the authorized vaccine, the authorization applicant is required to report the recall and submit pertinent product information relating to that recall to the DH and to comply with available guidance for pharmaceutical products, including the current Pharmaceutical Products Recall Guidelines issued by the Drug Office of the DH;
- (h) the authorization applicant is required to document any defect impacting the quality of the authorized vaccine released for sale or distribution;

- (i) the authorization applicant is required to submit further quality data to the DH at the same time when the said quality data or relevant quality documents reports are submitted to Canada, EU, UK or US drug regulatory authorities as part of its post-authorization commitments, and to update the relevant quality documents of the authorized vaccine, if applicable, in order to continue to assure the quality of the authorized vaccine;
- (j) the authorization applicant is required to ensure the authorized vaccine is distributed in accordance with the logistic plan as it has proposed;
- (k) the authorization applicant must provide the certificate of analysis issued by the manufacturer for each batch of the vaccine supplied to Hong Kong;
- (l) the authorization applicant should provide a lot release certificate issued by national regulatory authority (“NRA”) or batch release certificate issued by accredited laboratory authorized by NRA or certificate of analysis issued by an independent accredited laboratory for the batch of the vaccine supplied to Hong Kong as directed by the DH; and
- (m) the authorization applicant is required to submit relevant information and justifications / supporting evidence to the DH for any changes related to the authorized vaccine, including but not limited to the content of package insert, label, or any quality attributes. The changes should only be implemented after endorsement by the Secretary for Food and Health is obtained.

References:

1. Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020.
2. UK Medicines & Healthcare products Regulatory Agency. Public Assessment Report Authorisation for Temporary Supply COVID-19 mRNA Vaccine BNT162b2 (BNT162b2 RNA) concentrate for solution for injection. Available at https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/944544/COVID-19_mRNA_Vaccine_BNT162b2_UKPAR_PFIZER_BIONTECH_15Dec2020.pdf .
3. US Food and Drug Administration. Emergency Use Authorization for Pfizer-BioNTech COVID-19 Vaccine Review Memo. Available at <https://www.fda.gov/media/144416/download>.
4. EU European Medicines Agency. Comirnaty : EPAR – Product Information. Available at https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information_en.pdf.
5. EU European Medicines Agency. Comirnaty : EPAR – Public assessment report. Available at https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf .
6. EU European Medicines Agency. Comirnaty : EPAR – Risk-management-plan. Available at https://www.ema.europa.eu/en/documents/rmp/comirnaty-epar-risk-management-plan_en.pdf .
7. US Centers for Disease Control and Prevention. Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine – United States, December 14 – 23, 2020. Morbidity and Mortality Weekly Report January 2021.

COMIRNATY™ COVID-19 mRNA Vaccine (BNT162b2)

1. NAME OF THE MEDICINAL PRODUCT

COMIRNATY™ COVID-19 mRNA Vaccine (BNT162b2) concentrate for dispersion for injection

(hereinafter referred to as “COMIRNATY”)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multidose vial and must be diluted before use.
One vial (0.45 mL) contains 5 doses of 0.3mL after dilution.

1 dose (0.3 mL) contains 30 micrograms of COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).

Single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free *in vitro* transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for dispersion for injection (sterile concentrate).
The vaccine is a white to off-white frozen dispersion (pH: 6.9-7.9).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

COMIRNATY is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 16 years of age and older.

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Individuals 16 years of age and older

COMIRNATY is administered intramuscularly after dilution as a course of 2 doses (0.3 mL each) at least 21 days apart (see sections 4.4 and 5.1).

There are no data available on the interchangeability of COMIRNATY with other COVID-19 vaccines to complete the vaccination course. Individuals who have received 1 dose of COMIRNATY should receive a second dose of COMIRNATY to complete the vaccination course.

Paediatric population

The safety and efficacy of COMIRNATY in children and adolescents aged less than 16 years of age have not yet been established. Limited data are available.

Elderly population

No dosage adjustment is required in elderly individuals ≥ 65 years of age.

Method of administration

COMIRNATY should be administered intramuscularly.

The preferred site is the deltoid muscle of the upper arm.

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

General recommendations

Hypersensitivity and anaphylaxis

Events of anaphylaxis have been reported. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of COMIRNATY.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Immunocompromised individuals

The efficacy, safety and immunogenicity of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of COMIRNATY may be lower in immunosuppressed individuals.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical trials.

Limitations of vaccine effectiveness

As with any vaccine, vaccination with COMIRNATY may not protect all vaccine recipients. Individuals may not be fully protected until 7 days after their second dose of vaccine.

Excipients:

This vaccine contains less than 1 mmol potassium (39 mg) per dose, that is to say essentially 'potassium-free'.

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Concomitant administration of COMIRNATY with other vaccines has not been studied.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is limited experience with the use of COMIRNATY in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Administration of COMIRNATY in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

Breast-feeding

It is unknown whether COMIRNATY is excreted in human milk

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

4.7 Effects on ability to drive and use machines

COMIRNATY has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of safety profile

The safety of COMIRNATY was evaluated in participants 16 years of age and older in 2 clinical studies that included 21,744 participants that have received at least one dose of COMIRNATY.

In Study 2, a total of 21,720 participants 16 years of age or older received at least 1 dose of COMIRNATY and a total of 21,728 participants 16 years of age or older received placebo (including 138 and 145 adolescents 16 and 17 years of age in the vaccine and placebo groups, respectively). A total of 20,519 participants 16 years of age or older received 2 doses of COMIRNATY.

At the time of the analysis of Study 2, a total of 19,067 (9,531 COMIRNATY and 9,536 placebo) participants 16 years of age or older were evaluated for safety for at least 2 months after the second dose of COMIRNATY. This included a total of 10,727 (5,350 COMIRNATY and 5,377 placebo) participants 16 to 55 years of age and a total of 8,340 (4,181 COMIRNATY and 4,159 placebo) participants 56 years and older.

The most frequent adverse reactions in participants 16 years of age and older were injection site pain (> 80%), fatigue (> 60%), headache (> 50%), myalgia and chills (> 30%), arthralgia (> 20%), pyrexia and injection site swelling (> 10%) and were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

Tabulated list of adverse reactions from clinical studies

Adverse reactions observed during clinical studies are listed below according to the following frequency categories:

Very common ($\geq 1/10$),

Common ($\geq 1/100$ to $< 1/10$),

Uncommon ($\geq 1/1,000$ to $< 1/100$),

Rare ($\geq 1/10,000$ to $< 1/1,000$),

Very rare ($< 1/10,000$),

Not known (cannot be estimated from available data).

Table 1: Adverse reactions from COMIRNATY clinical trials

System Organ Class	Very common ($\geq 1/10$)	Common ($\geq 1/100$ to $< 1/10$)	Uncommon ($\geq 1/1,000$ to $< 1/100$)	Rare ($\geq 1/10,000$ to $< 1/1,000$)	Not known (cannot be estimated from the available data)
Blood and lymphatic system disorders			Lymphadenopathy		
Immune system disorders					Anaphylaxis; hypersensitivity
Psychiatric disorders			Insomnia		
Nervous system disorders	Headache			Acute peripheral facial paralysis†	
Gastrointestinal disorders		Nausea			
Musculoskeletal and connective tissue disorders	Arthralgia; myalgia		Pain in extremity		
General disorders and administration site conditions	Injection site pain; fatigue; chills; pyrexia*; injection site swelling	Injection site redness	Malaise; injection site pruritus		

*A higher frequency of pyrexia was observed after the 2nd dose.

†Throughout the safety follow-up period to date, acute peripheral facial paralysis (or palsy) was reported by four participants in the COVID-19 mRNA Vaccine group. Onset was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of acute peripheral facial paralysis (or palsy) were reported in the placebo group.

The safety profile in 545 subjects receiving COMIRNATY, that were seropositive for SARS-CoV-2 at baseline, was similar to that seen in the general population.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to local regulatory authorities per local requirements.

Alternatively, healthcare professionals can also contact respective company representatives of local suppliers/distributors for assistance in such reporting.

4.9 Overdose

Overdose data is available from 52 study participants included in the clinical trial that due to an error in dilution received 58 micrograms of COMIRNATY. The vaccine recipients did not report an increase in reactogenicity or adverse reactions.

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccines, ATC code: J07BX

Mechanism of action

The nucleoside-modified messenger RNA in COMIRNATY is formulated in lipid nanoparticles, which enable delivery of the non replicating RNA into host cells to direct transient expression of the SARS- CoV-2 S antigen. The mRNA codes for membrane-anchored, full-length S with two point mutations within the central helix. Mutation of these two amino acids to proline locks S in an antigenically preferred prefusion conformation. The vaccine elicits both neutralizing antibody and cellular immune responses to the spike (S) antigen, which may contribute to protection against COVID-19.

Efficacy

Study 2 is a multicentre, multinational, Phase 1/2/3 randomised, placebo-controlled, observer-blind dose-finding, vaccine candidate selection and efficacy study in participants 12 years of age and older. Randomisation was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥ 56 -year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with pre-existing stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrolment, were included as were participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV) or hepatitis B virus (HBV). At the time of the analysis of Study 2, information presented is based on participants 16 years and older.

Efficacy in participants 16 years of age and older

In the Phase 2/3 portion, approximately 44,000 participants were randomised equally and were to receive 2 doses of COVID-19 mRNA Vaccine or placebo separated by 21 days. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. Participants are planned to be followed for up to 24 months after Dose 2, for assessments of safety and efficacy against COVID-19. In the clinical study, participants were required to observe a minimum interval of 14 days before and after administration of an influenza vaccine in order to receive either placebo or COVID-19 mRNA Vaccine. In the clinical study, participants were required to observe a minimum interval of 60 days before or after receipt of blood/plasma products or immunoglobulins within through conclusion of the study in order to receive either placebo or COVID-19 mRNA Vaccine.

The population for the analysis of the primary efficacy endpoint included, 36,621 participants 12 years of age and older (18,242 in the COVID-19 mRNA Vaccine group and 18,379 in the placebo group) who did not have evidence of prior infection with SARS-CoV-2 through 7 days after the second dose. In addition, 134 participants were between the ages of 16 to 17 years of age (66 in the COVID-19 mRNA Vaccine group and 68 in the placebo group) and 1616 participants 75 years of age and older (804 in the COVID-19 mRNA Vaccine group and 812 in the placebo group).

Efficacy against COVID-19

At the time of the primary efficacy analysis, participants had been followed for symptomatic COVID-19 for in total 2,214 person-years for the COVID-19 mRNA Vaccine and in total 2,222 person-years in the placebo group.

There were no meaningful clinical differences in overall vaccine efficacy in participants who were at risk of severe COVID-19 including those with 1 or more comorbidities that increase the risk of severe COVID-19 (e.g. asthma, body mass index (BMI) ≥ 30 kg/m², chronic pulmonary disease, diabetes mellitus, hypertension).

The vaccine efficacy information is presented in Table 2.

Table 2: Vaccine efficacy – First COVID-19 occurrence from 7 days after Dose 2, by age subgroup – participants without evidence of infection prior to 7 days after Dose 2 – evaluable efficacy (7 days) population

First COVID-19 occurrence from 7 days after Dose 2 in participants without evidence of prior SARS-CoV-2 infection*			
Subgroup	COVID-19 mRNA Vaccine N ^a = 18,198 Cases n1 ^b Surveillance time ^c (n2 ^d)	Placebo N ^a = 18,325 Cases n1 ^b Surveillance time ^c (n2 ^d)	Vaccine efficacy % (95% CI) ^f
All subjects ^e	8 2.214 (17,411)	162 2.222 (17,511)	95.0 (90.0, 97.9)
16 to 64 years	7 1.706 (13,549)	143 1.710 (13,618)	95.1 (89.6, 98.1)
65 years and older	1 0.508 (3848)	19 0.511 (3880)	94.7 (66.7, 99.9)
65 to 74 years	1 0.406 (3074)	14 0.406 (3095)	92.9 (53.1, 99.8)
75 years and older	0 0.102 (774)	5 0.106 (785)	100.0 (-13.1, 100.0)

Note: Confirmed cases were determined by Reverse Transcription-Polymerase Chain Reaction (RT-PCR) and at least 1 symptom consistent with COVID-19 [*Case definition: (at least 1 of) fever, new or increased cough, new or increased shortness of breath, chills, new or increased muscle pain, new loss of taste or smell, sore throat, diarrhoea or vomiting.]

* Participants who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (i.e., N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by nucleic acid amplification tests (NAAT) [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of participants in the specified group.

b. n1 = Number of participants meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. No confirmed cases were identified in participants 12 to 15 years of age.

f. Confidence interval (CI) for vaccine efficacy is derived based on the Clopper and Pearson method adjusted to the surveillance time. CI not adjusted for multiplicity.

In the second primary analysis, compared to placebo, efficacy of COVID-19 mRNA Vaccine in participants from first COVID-19 occurrence from 7 days after Dose 2 compared to participants with or without evidence of prior infection with SARS-CoV-2 was 94.6% (95% credible interval of 89.9% to 97.3%) in participants 16 years of age and older.

Additionally, subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, racial and ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19.

Paediatric population

Further evidence is awaited.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeat dose toxicity and reproductive and developmental toxicity.

General toxicity

Rats intramuscularly administered COMIRNATY (receiving 3 full human doses once weekly, generating relatively higher levels in rats due to body weight differences) demonstrated some injection site oedema and erythema and increases in white blood cells (including basophils and eosinophils) consistent with an inflammatory response as well as vacuolation of portal hepatocytes without evidence of liver injury. All effects were reversible.

Genotoxicity/Carcinogenicity

Neither genotoxicity nor carcinogenicity studies were performed. The components of the vaccine (lipids and mRNA) are not expected to have genotoxic potential.

Reproductive toxicity

Reproductive and developmental toxicity were investigated in rats in a combined fertility and developmental toxicity study where female rats were intramuscularly administered COMIRNATY prior to mating and during gestation (receiving 4 full human doses that generate relatively higher levels in rat due to body weight differences, spanning between pre-mating day 21 and gestational day 20). SARS-CoV-2 neutralizing antibody responses were present in maternal animals from prior to mating to the end of the study on postnatal day 21 as well as in foetuses and offspring. There were no vaccine-related effects on female fertility, pregnancy, or embryo-foetal or offspring development. No COMIRNATY data are available on vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

(4-hydroxybutyl) azanediyl)bis (hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)

2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)

1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC)

Cholesterol,

Potassium chloride

Potassium dihydrogen phosphate

Sodium chloride

Disodium hydrogen phosphate dihydrate

Sucrose

Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal

products except those mentioned in section 6.6.

6.3 Shelf life

Unopened vial: 6 months at -90 °C to -60 °C.

Once removed from the freezer, the unopened vaccine can be stored for up to 5 days at 2 °C to 8 °C, and up to 2 hours at temperatures up to 30 °C, prior to use.

Once thawed, the vaccine should not be re-frozen.

Closed-lid vial trays containing 195 vials removed from frozen storage (< -60 °C) may be at room temperature (< 25 °C) for up to 5 minutes for transfer between ultra-low-temperature environments. After vial trays are returned to frozen storage following room temperature exposure, they must remain in frozen storage for at least 2 hours before they can be removed again.

Diluted medicinal product

Chemical and physical in-use stability has been demonstrated for 6 hours at 2 °C to 30 °C after dilution in sodium chloride 9 mg/mL (0.9%) solution for injection. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Store at -90°C to -60°C.

Store in the original package in order to protect from light.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Thawed vials can be handled in room light conditions.

When you are ready to thaw or use the vaccine

- Open-lid vial trays, or vial trays containing less than 195 vials removed from frozen storage (< -60 °C) may be at room temperature (< 25 °C) for up to 3 minutes to remove vials or for transfer between ultra-low-temperature environments.
- Once a vial is removed from the vial tray, it should be thawed for use.
- After vial trays are returned to frozen storage following room temperature exposure, they must remain in frozen storage for at least 2 hours before they can be removed again.

For storage conditions after thawing and dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

2 mL clear multidose vial (type I glass) with a stopper (synthetic bromobutyl rubber) and a flip-off plastic cap with aluminium seal. Each vial contains 5 doses.

Pack sizes: 1, 5 or 195 vials per box.

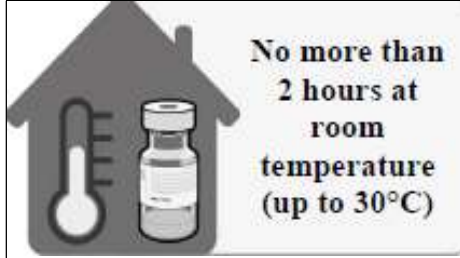
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Handling instructions

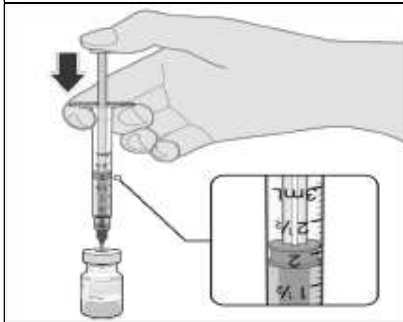
COMIRNATY should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared dispersion.

THAWING PRIOR TO DILUTION

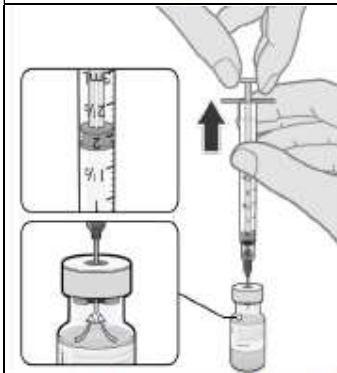


- The multidose vial is stored frozen and must be thawed prior to dilution. Frozen vials should be transferred to an environment of 2 °C to 8 °C to thaw; a 195 vial pack may take 3 hours to thaw. Alternatively, frozen vials may also be thawed for 30 minutes at temperatures up to 30 °C for immediate use.
- Allow the thawed vial to come to room temperature and gently invert it 10 times prior to dilution. Do not shake.
- Prior to dilution, the thawed dispersion may contain white to off-white opaque amorphous particles.

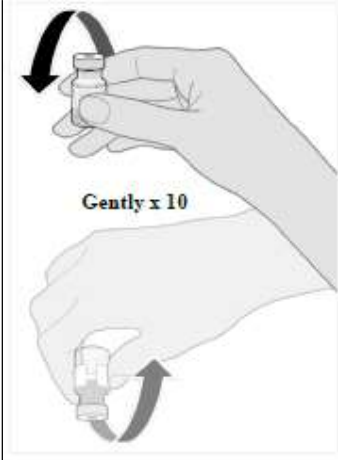

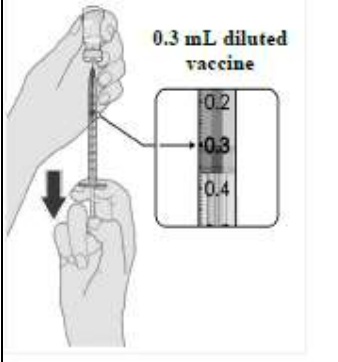
DILUTION



- The thawed vaccine must be diluted in its original vial with 1.8 mL sodium chloride 9 mg/mL (0.9%) solution for injection, using a 21 gauge or narrower needle and aseptic techniques.



- Equalise vial pressure before removing the needle from the vial stopper by withdrawing 1.8 mL air into the empty diluent syringe.

	<ul style="list-style-type: none"> • Gently invert the diluted dispersion 10 times. Do not shake. • The diluted vaccine should present as an off-white dispersion with no particulates visible. Discard the diluted vaccine if particulates or discoloration are present.
	<ul style="list-style-type: none"> • The diluted vials should be marked with the appropriate date and time. • Do not freeze or shake the diluted dispersion. If refrigerated, allow the diluted dispersion to come to room temperature prior to use.
PREPARATION OF INDIVIDUAL 0.3 mL DOSES OF COMIRNATY	
	<ul style="list-style-type: none"> • After dilution, the vial contains 2.25 mL corresponding to 5 doses of 0.3 mL. Withdraw the required 0.3 mL dose of diluted vaccine using a sterile needle. • Discard any unused vaccine within 6 hours after dilution.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. DATE OF REVISION OF THE TEXT

December 2020.

Package leaflet: Information for the user

**Comirnaty concentrate for dispersion for injection
COVID-19 mRNA Vaccine (BNT162b2)**

Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Comirnaty is and what it is used for
2. What you need to know before you receive Comirnaty
3. How Comirnaty is given
4. Possible side effects
5. How to store Comirnaty
6. Contents of the pack and other information

1. What Comirnaty is and what it is used for

Comirnaty is a vaccine used for preventing COVID-19 caused by SARS-CoV-2 virus.

Comirnaty is given to adults and adolescents from 16 years of age and older.

The vaccine causes the immune system (the body's natural defences) to produce antibodies and blood cells that work against the virus, so giving protection against COVID-19.

As Comirnaty does not contain the virus to produce immunity, it cannot give you COVID-19.

2. What you need to know before you receive Comirnaty

Comirnaty should not be given

- if you are allergic to the active substance or any of the other ingredients of this medicine (listed in section 6)

Warnings and precautions

Talk to your doctor, pharmacist or nurse before you are given the vaccine if:

- you have ever had a severe allergic reaction or breathing problems after any other vaccine injection or after you were given Comirnaty in the past.
- you have ever fainted following any needle injection.
- you have a severe illness or infection with high fever. However, you can have your vaccination if you have a mild fever or upper airway infection like a cold.
- you have a bleeding problem, you bruise easily or you use a medicine to prevent blood-clots.
- you have a weakened immune system, because of a disease such as HIV infection or a medicine such as corticosteroid that affects your immune system

As with any vaccine, the 2-dose vaccination course of Comirnaty may not fully protect all those who receive it and it is not known how long you will be protected.

Children and adolescents

Comirnaty is not recommended for children aged under 16 years.

Other medicines and Comirnaty

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines or have recently received any other vaccine.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before you receive this vaccine.

Driving and using machines

Some of the effects of vaccination mentioned in section 4 (Possible side effects) may temporarily affect your ability to drive or use machines. Wait until these effects have worn off before you drive or use machines.

Comirnaty contains potassium and sodium

This vaccine contains less than 1 mmol potassium (39 mg) per dose, that is to say essentially 'potassium-free'.

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How Comirnaty is given

Comirnaty is given after dilution as an injection of 0.3 mL into a muscle of your upper arm.

You will receive 2 injections, given at least 21 days apart.

After the first dose of Comirnaty, you should receive a second dose of the same vaccine after 21 days to complete the vaccination course.

If you have any further questions on the use of Comirnaty, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all vaccines, Comirnaty can cause side effects, although not everybody gets them.

Very common side effects: may affect more than 1 in 10 people

- injection site: pain, swelling
- tiredness
- headache
- muscle pain
- joint pain
- chills, fever

Common side effects: may affect up to 1 in 10 people

- injection site redness
- nausea

Uncommon side effects: may affect up to 1 in 100 people

- enlarged lymph nodes
- feeling unwell

- pain in limb
- insomnia
- injection site itching

Rare side effects: may affect up to 1 in 1,000 people

- temporary one sided facial drooping

Not known (cannot be estimated from the available data)

- severe allergic reaction

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the local reporting system and include batch/Lot number if available. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Comirnaty

Keep this medicine out of the sight and reach of children.

The following information about storage, expiry and use and handling is intended for healthcare professionals.

Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Store in freezer at -90 °C to -60 °C.

Store in the original package in order to protect from light.

After thawing, the vaccine should be diluted and used immediately. However, in-use stability data have demonstrated that once removed from freezer, the undiluted vaccine can be stored for up to 5 days at 2 °C to 8 °C, or up to 2 hours at temperatures up to 30 °C, prior to use.

After dilution, store the vaccine at 2 °C to 30 °C and use within 6 hours. Discard any unused vaccine.

Once removed from the freezer and diluted, the vials should be marked with the new discard date and time. Once thawed, the vaccine cannot be re-frozen.

Do not use this vaccine if you notice particulates in the dilution or discolouration.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Comirnaty contains

- The active substance is COVID-19 mRNA Vaccine. After dilution, the vial contains 5 doses of 0.3 mL with 30 micrograms mRNA each.
- The other ingredients are: – ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)

- 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)
- 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC)
- cholesterol
- potassium chloride
- potassium dihydrogen phosphate
- sodium chloride
- disodium phosphate dihydrate
- sucrose
- water for injections

What Comirnaty looks like and contents of the pack

The vaccine is a white to off-white dispersion (pH: 6.9 - 7.9) provided in a multidose vial of 5 doses in a 2 mL clear vial (type I glass), with a rubber stopper and a flip-off plastic cap with aluminium seal.
Pack size: 195 vials, 5 vials, 1 vial

Revision date: December 2020

藥品說明書：使用者須知

Comirnaty 注射用分散體濃縮液

COVID-19 mRNA 疫苗 (BNT162b2)

本說明書包含重要資訊，在接種本疫苗前請仔細閱讀本藥品說明書的全部內容。

- 請保留本說明書。您可能需要再次閱讀。
- 如有其他任何疑問，請諮詢醫生、藥劑師或護士。
- 如果出現任何副作用，請告知醫生、藥劑師或護士。這包括本說明書未列出的任何可能的副作用。請參見第 4 節。

本說明書中有甚麼內容

1. 甚麼是 Comirnaty 及其用途
2. 在使用 Comirnaty 前，需要瞭解甚麼事項
3. 如何給予 Comirnaty
4. 可能出現的副作用
5. 如何儲存 Comirnaty
6. 包裝內容物和其他資訊

1. 甚麼是 Comirnaty 及其用途

Comirnaty 是一種適用於預防由 SARS-CoV-2 病毒引起的 COVID-19 的疫苗。

成人和 16 歲及以上的青少年可接種 Comirnaty。

本疫苗可使免疫系統（人體的天然防禦系統）產生對抗該病毒的抗體和血細胞，從而預防 COVID-19。

由於 Comirnaty 不含有產生免疫力的病毒，故不會導致 COVID-19。

2. 在使用 Comirnaty 前，需要瞭解甚麼事項

不應給予 Comirnaty

- 如果您對藥物的活性物質或其他成分有過敏反應（見第 6 節）。

警告和注意事項

如果您有以下情況，使用本疫苗前，請諮詢您的醫生、藥劑師或護士：

- 以往在接種 Comirnaty 或任何其他疫苗後，您曾出現過嚴重過敏反應或呼吸問題。

- 您曾在任何針頭注射後暈倒。
- 您患有嚴重疾病或伴有高燒的感染。但是，如果您出現輕微發燒或上呼吸道感染（如感冒），您可以接種本疫苗。
- 您有出血問題，容易出現瘀青或正在使用預防血凝塊的藥物。
- 由於 HIV 感染等疾病或影響免疫系統的藥物（如皮質類固醇），您的免疫系統減弱。

與任何疫苗一樣，接種 2 劑 Comirnaty 疫苗後可能無法保護所有接種 Comirnaty 的患者，尚不清楚您將受到多長時間的保護。

兒童和青少年

Comirnaty 不推薦用於 16 歲以下的兒童。

其他藥物和 Comirnaty

如果你正使用、最近已經使用或可能需要使用其他藥物或近期接種過任何其他疫苗，請告知您的醫生或藥劑師。

懷孕和哺乳

如果您正在懷孕或哺乳、認為您可能懷孕或計畫懷孕，在接種本疫苗前請向您的醫生或藥劑師徵求意見。

駕駛車輛和操作機器

第 4 節（可能的副作用）中提到的疫苗接種的某些影響可能會暫時影響您的駕駛車輛或操作機器的能力。請在這些影響消失後再駕駛車輛或操作機器。

Comirnaty 含有鉀和鈉

本疫苗每劑含 <1 mmol (39 mg) 的鉀，即基本上「無鉀」。

本疫苗每劑含 <1 mmol (23 mg) 的鈉，即基本上「無鈉」。

3. 如何給予 Comirnaty

稀釋後，在您上臂肌肉內注射 0.3 mL Comirnaty。

您將接受 2 次注射，至少間隔 21 天。

接種第 1 劑 Comirnaty 後，您應在 21 天後接種第 2 劑相同的疫苗，以完成疫苗接種。

關於 Comirnaty 使用，如還有任何疑問，請諮詢您的醫生、藥劑師或護士。

4. 可能出現的副作用

與所有疫苗一樣，Comirnaty 可能引起副作用，但並非所有人均會出現副作用。

非常常見的副作用：可能影響患者比例 >1/10

- 注射部位：疼痛、腫脹
- 疲倦

- 頭痛
- 肌肉痛
- 關節痛
- 寒顫、發燒

常見副作用：可能影響患者比例 $\leq 1/10$

- 注射部位發紅
- 噁心

不常見副作用：可能影響患者比例 $\leq 1/100$

- 淋巴結腫大
- 感覺不適
- 肢體疼痛
- 失眠
- 注射部位發癢

罕見副作用：可能影響患者比例 $\leq 1/1,000$

- 暫時性一側面部下垂

未知（無法根據現有資料估算）

- 嚴重過敏反應

副作用的報告

如果出現任何副作用，請告知醫生、藥劑師或護士。這包括本說明書內未列出的任何可能的副作用。您也可以通過本地呈報系統直接呈報副作用，如適用，應標明批號。通過呈報副作用，您可以幫助提供關於本藥品安全性的更多資訊。

5. 如何儲存 Comirnaty

請將本品放置在兒童不可見且接觸不到的地方。

以下有關儲存、有效期、使用和處理的資訊僅供專業醫護人員使用。

在包裝盒和標籤上註明的有效期過後，請勿使用本品。有效期是指當月的最後一天。

在冷凍櫃 -90°C 至 -60°C 保存。

在原包裝中避光儲存。

本疫苗在解凍後，應立即稀釋及使用。然而，使用期間穩定性資料表明，一旦從冷凍櫃中取出後，未稀釋疫苗在使用前可在 2°C - 8°C 儲存最多5天，或在最高 30°C 的環境儲存最多2小時。

疫苗在稀釋後，於 2°C-30°C 儲存，並在 6 小時內使用。應丟棄任何未使用的疫苗。

一旦從冷凍櫃中取出並稀釋後，應在小瓶上標記新的丟棄日期和時間。本疫苗在解凍後不得重新冷凍。

如果發現本疫苗在稀釋後有顆粒物或變色，請勿使用。

請勿通過污水或家居垃圾處理任何藥物。向您的藥劑師諮詢如何丟棄您不再使用的藥物。這些措施將有助於保護環境。

6. 包裝內容物和其他資訊

Comirnaty 所含成分

- 活性物質為 COVID-19 mRNA 疫苗。稀釋後，每小瓶含 5 個 0.3 mL 劑量，每劑含 30 µg mRNA。
- 其他成分包括：
 - ((4-羥丁基)氮雜二基)雙(己烷-6,1-二基)雙(2-己基癸酸酯) (ALC-0315)
 - 2-[(聚乙二醇)-2000]-N,N-二十四烷基乙醯胺 (ALC-0159)
 - 1,2-二硬脂醯-sn-甘油-3-磷酸膽鹼 (DSPC)
 - 膽固醇
 - 氯化鉀
 - 磷酸二氫鉀
 - 氯化鈉
 - 磷酸氫二鈉二水合物
 - 蔗糖
 - 注射用水
- 英文名稱為：
 - - ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)
 - - 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)
 - - 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC)
 - - cholesterol
 - - potassium chloride
 - - potassium dihydrogen phosphate
 - - sodium chloride
 - - disodium phosphate dihydrate
 - - sucrose
 - - water for injections

Comirnaty 外觀和包裝內容物

疫苗為白色至類白色分散體（pH：6.9-7.9），裝於 2 mL 透明多劑小瓶（I類玻璃瓶）中，每瓶含 5 劑，配有橡膠瓶塞並用鋁塑易掀蓋密封。

包裝規格：195 個小瓶裝、5 個小瓶裝、1 個小瓶裝。

修訂日期:2020 年 12 月